The third case was one of typhoid fever, toward the end of the second week. The temperature was between 103 and 104° F. The blood culture showed, in 10 c.c. of blood, 102 pure colonies of typhoid bacilli. The typhoid colonies appeared as blackish spots and points, visible after twenty-four hours incubation. Within the next twenty-four hours part of them reached the surface where they spread as a well-circumscribed shining growth, showing a peculiar grayish (mouse-gray) color.

The pneumococcus has been found by Lenhartz in grave cases of pneumonia in 20 per cent. of the cases. As to the appearance of its growth it may only be mentioned here that the macroscopic appearance of the colonies in blood-agar plates closely resembles that of the streptococcus varieties, but the halo of decoloration surrounding the single colonies which appear as black wheat-stone shaped spots of about 0.5 mm. in length is not clear as in the case of the streptococcus, but shows a distinct greenish hue.

OBSERVATIONS UPON CERTAIN BLOOD-PRESSURE-LOWERING REFLEXES THAT ARISE FROM IRRITATION OF THE INFLAMED PLEURA.

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Thoracentesis and all operative procedures inside the thoracic cavity where inflammation exists may be accompanied or followed by disturbances of circulation. These occur even when such complications as pulmonary œdema, accidental hemorrhage, and pneumothorax can be definitely excluded. As a rule these disturbances are trivial and consist of lowering of arterial tension accompanied by faintness. Occasionally, however, the symptoms are serious. Without warning the patient becomes dyspnœic and cyanotic, and the pulse is thready, with a tension below the safety point. Unconsciousness and death may supervene in a few minutes or in a few hours.

The cause of death in these cases is usually not discovered by the pathologist. Rarely emboli or thrombi are found in the heart or pulmonary arteries and even more rarely in the cerebral arteries

(Rosenbach). After excluding such exceptional conditions there still remains a considerable number of cases of sudden death in which *no anatomical lesion can be found postmortem to explain the collapse.*

Rosenbach[1] considers that the chief factors in producing death in these obscure cases are anemia of the heart or brain, sudden heart-failure, or a reflex inhibition of the respiratory and cardiac centres. Russell[2] believes that the pulmonary fibers of the vagus nerve, made sensitive by inflammation, carry impulses to the medulla. The impulses originate, he thinks, in the alveoli and not in the pleura.

In a series of recent observations by one of us[3] upon the blood pressure in aspirating pleural effusions, it was concluded that the *rapidity of withdrawal,* the removal of a *large amount* of fluid, the presence of a *long-standing effusion* and of *senile changes* in the heart and bloodvessels, were the chief factors in bringing about a marked fall of arterial blood pressure with unfavorable symptoms. All these, however, are contributing causes only and fail to explain the mechanism of the phenomena.

The following experiments were made with the purpose of finding out if possible the nature of this mechanism:

GROUP I.—*Aspiration of Oil from the Normal Pleural Cavity.* All the dogs under this group were injected in one pleural cavity with sterile cotton-seed oil, which, unlike watery solutions, is not absorbed by the pleural membrane. The fluid was allowed to flow in until the first signs of dyspnœa developed. Readings of the blood pressure were taken before, during, and after aspiration.

EXPERIMENT 1. 700 c.c. cotton-seed oil injected into left pleural cavity of large dog. 500 c.c. withdrawn in the period of five minutes:

Initial blood pressure	130 mm. Hg.
After injection of 700 c.c. of oil	140 "
Immediately after aspiration of 500 c.c.	115 "
Final blood pressure ten minutes after aspiration	120 "

EXPERIMENT 2. Medium-sized dog:

Initial blood pressure	132 mm. Hg.
After injection of 500 c.c. of oil in left pleural cavity	138 "
After aspiration of 400 c.c.	134 "
Final blood pressure eight minutes later	130 "

EXPERIMENT 3. Large dog:

Initial blood pressure	128 mm. Hg.
After injection of 750 c.c. of oil in right pleural cavity	148 "
After aspiration of 550 c.c.	140 "
Final blood pressure five minutes later	125 "

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[1] Nothnagel's Encyclopedia of Medicine, 1903.

[2] St. Thomas' Hospital Reports, 1899, vol. xxviii.

[3] Capps, Jour. Amer. Med. Assoc., January 5, 1907.

EXPERIMENT 4. Rather small dog:

Two days after injection of 450 c.c. sterile oil in right pleural cavity	100 mm. Hg.
After rapid aspiration of 350 c.c.	120 "
Final blood pressure	100 "

No pleurisy found postmortem.

EXPERIMENT 5. Medium-sized dog:

Initial blood pressure	70 mm. Hg.
After injection of 600 c.c. of oil in right pleural cavity	80 "
After aspiration of 450 c.c	70 "
Final blood pressure ten minutes later	70 "

EXPERIMENT 6. Dog of large size:

Initial blood pressure	100 mm. Hg.
After injection of 600 c.c. of oil in left pleural cavity	110 "
After aspiration of 350 c.c.	95 "
Final blood pressure ten minutes later	97 "

Discussion. The average rise in blood pressure in these six cases produced by injecting the oil was about 12 mm. Hg. The average fall in pressure as a result of aspiration was 11 mm. Hg. The rise in pressure accompanying the introduction of fluid may be attributed to the diminution of lung space and to pressure exerted by the weight of the fluid on the lungs, the heart, and the neighboring vessels. The fall in pressure following aspiration may be referred to the restoration of physiological conditions. There was no evidence of any reflex disturbance of circulation during aspiration, such as transitory falls in pressure or changes in the pulse rate.

GROUP II.—*Aspiration of Exudates in Artificial Pleurisy.* The pleurisy was created by injecting from 10 to 300 c.c. of cotton-seed oil contaminated with bacteria in one pleural cavity of a dog. At the end of twenty-four to forty-eight hours a bilateral pleurisy had developed, with a thick pleural exudate and a large amount of free fluid on the injected side; on the opposite side, a thinner pleural exudate and very little free fluid. The fluid was aspirated with a water pump as rapidly as possible.

EXPERIMENT 7. Bilateral pleurisy in a dog which had been injected forty-eight hours before with 10 c.c. of dirty oil in the right chest:

Blood pressure before aspiration	130 mm. Hg.
After aspiration of 150 c.c. of oil and exudate	110 "
Ten minutes later	115 "

EXPERIMENT 8. Dog with marked right pleurisy twenty-four hours after injection of 200 c.c. of oil in right side; left pleura congested:

Blood pressure before aspiration	90 mm. Hg.
After aspiration of 150 c.c.	70 "
Six minutes later	74 "

EXPERIMENT 9. Dog injected forty-eight hours previously in right pleural cavity with 300 c.c. of dirty oil. Right pleurisy moderate, left slight:

Initial blood presssure	110 mm. Hg.
After aspiration of 200 c.c.	110 "
Five minutes later	110 "

Experiment 10. Bilateral pleurisy in dog injected in left side forty-eight hours before with 225 c.c. of oil:

Initial blood pressure	130 mm. Hg.
After aspiration of 150 c.c.	130 "
Six minutes later	130 "

Experiment 11. Bilateral pleurisy forty-eight hours after introduction of 200 c.c. of oil in right pleural cavity:

Initial blood pressure	110 mm. Hg.
After aspiration of 150 c.c.	100 "
Eight minutes later	105 "

Experiment 12. Bilateral pleurisy forty-eight hours after injection of 200 c.c. of oil:

Initial blood pressure	120 mm. Hg.
After aspiration of 100 c.c.	100 "
Five minutes later	105 "

Experiment 13. Bilateral pleurisy forty-eight hours after introduction of 200 c.c. of oil into right cavity:

Initial blood pressure	140 mm. Hg.
After rapid aspiration of 100 c.c.	30 "
Three minutes later	Death.

During the process of aspiration in this experiment the respiration slowed and finally ceased altogether, although the ether was withdrawn.

Discussion. It should be noted that the average amount of exudate withdrawn in this group was about 150 c.c., while the average quantity in Group I was about 500 c.c. We should expect less of a fall in pressure, therefore, in Group II from purely pressure effects. As a matter of fact, the results were about the same in the two groups, which would indicate that aspiration of a small quantity of fluid from an inflamed pleural cavity may produce as much lowering of tension as a much larger quantity of fluid from a normal cavity. Transitory changes in pressure were common during these experiments, and especially in the last one it was observed that the movement of the trocar on the pleura sometimes caused a marked fall in blood pressure, even when the amount of fluid aspirated was small. We were thereby led to investigate the effect produced on blood pressure by irritation of the pleura, healthy and inflamed, independently of aspiration.

Group III. *Irritation of Healthy Pleura.* The procedure in these experiments was as follows:

The dog was etherized and laid on the operating table. The trachea was opened and a cannula inserted which connected with a flask of ether. By means of a T-glass cannula in this connecting tube a smaller tube was attached that carried the air waves to a recording tambour. The blood-pressure tracings were made by means of a mercury manometer connected with the carotid artery.

A trocar was inserted in the mid- or post-axillary line, fifth or sixth interspace, and the sharp point withdrawn. A scratching movement of the blunt trocar was made, then a similar movement with the sharp point. Formalin (3 to 5 drops) was then blown upon the visceral surface of the pleura by inserting a long glass tube through the trocar, precautions being taken to avoid entrance of air. These experiments were then repeated on the opposite side. In six of the nine dogs in the group the chest was laid open by cutting through the midsternal line and artificial respiration was maintained. We were then enabled to try chemical, thermal, and electrical forms of irritation at various parts of both the parietal and visceral pleura, the pericardium, and the nerve branches themselves.

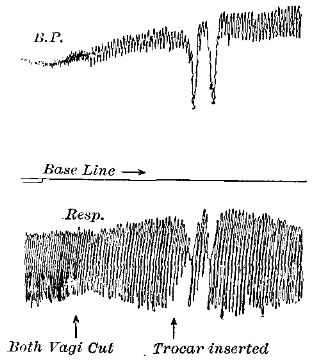

FIG. 1.—Effect of forcing a trocar through the chest wall into the pleural cavity of a normal dog. Note the transitory drops in blood pressure and disturbance of respirations. Section of both vagus nerves in the neck does not alter the reaction The fall in pressure is greatest at the moment the *parietal* pleura is pierced.

As the results were so nearly uniform, Experiments 13 to 22 may be briefly summarized. Mechanical irritation of the visceral pleura with a dull instrument was always negative; with a sharp point there was either very slight or no reaction. Only once did chemical irritation produce a reaction, and that was slight. Formalin was nearly always employed. Bromine and ammonia, which were occasionally used, also had no effect upon blood pressure. Thermal irritation was tested by means of a hot iron or a piece of ice held in the forceps. All tests were negative. Electrical stimulation with the induced current did not affect blood pressure unless a strong current was applied to the roots of the lung, in which location inhibitory effects on the heart were elicited.

Quite constantly a transitory fall in pressure and a checking of respiration accompanied the penetration of the perietal pleura with the trocar (Fig. 1).

It should be added that either mechanical or electrical stimulation of the pericardium is likely to set up a cardio-inhibitory reflex when the membrane lies upon the heart. If the pericardium is separated, however, from the heart muscle, no effect follows such irritation. The reflex, therefore, is a stimulation of the cardiac nerves transmitted through the pericardium. Any violence to the heart by sudden displacement or accidental contact of the trocar may give rise to such a reflex, which, fortunately, is transitory and does not cause a lasting change in blood pressure.

These results confirm the excellent series of observations by Brodie and Russell[4] on the healthy lungs of dogs. They found the pulmonary fibers at the root of the lung and in the bronchial tubes and alveoli would respond to electrical stimulation with a more powerful cardio-inhibitory action than any other branches of the vagus nerve. In addition to this effect on the heart they found that strong excitation of the pulmonary fibers, as by the inhalation of formalin, acted also on the respiratory and vasomotor centres. Since they found no effect on blood pressure from stimulation of the healthy pleural membrane except where the nerves enter the lung, Russell assumed that no reflexes arise from the diseased pleura.

Such an assumption, however, is not justified, because an inflamed nerve may be sensitive to irritants to which the healthy nerve is not sensitive, and consequently the inflamed nerve may cause reflexes which the healthy nerve does not induce. A reflex of this type is pathological.

An illustration of this principle is afforded by the recent experiments of Buerger and Churchman.[5] They found that electrical excitation of the cœliac plexus in healthy animals produced no bad results. Similar excitation of the plexus after a peritonitis had been produced by injection of turpentine caused collapse and death, either during or after the operation. It was assumed therefore that the inflammation rendered the nerves abnormally susceptible to the conduction of reflexes causing vasodilatation.

Bearing in mind these possibilities we tried various forms of stimulation of the pleura in a series of animals in which varying degrees of pleuritis had been produced by different forms of irritants.

GROUP IV.—*Irritation of Inflamed Pleura.* An artificial pleurisy was set up by two methods. The first consisted of injecting a few cubic centimeters of turpentine mixed with cotton-seed oil. At the end of six hours flakes of fibrin were visible over the congested pleural surface; in twenty-four hours there was a fairly thick membrane and an accumulation of fluid exudate. The opposite side was usually not involved.

The second method was carried out by injecting in the chest 10 to

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[4] Jour. Phys., 1900, vol. xxvi, p. 92.

[5] Mitteil. d. Grenzgeb. d. Med. u. Chir., 1906, vol. xvi,

200 c.c. of cotton-seed oil contaminated with bacteria. In twenty-four hours the pleural surface was covered with a fibrinous film and a few flakes were often found on the opposite side. After forty-eight hours the inoculated side presented a dense, fibrinous exudate with fluid accumulation, while the opposite pleura was overlaid by a thin, fibrinous exudate, accompanied by a variable amount of free fluid.

Since the chemically produced pleuritis develops more quickly, animals so treated were employed from six to twenty-four hours after injection. The animals inoculated with the more slowly developing bacterial injection were subjected to experiment twenty-four to seventy-two hours after the injection.

It seemed desirable to test the pleura under various degrees and varieties of inflammation as well as to compare in the same animal the effect of irritation of the highly inflamed pleura of one side with the slightly inflamed pleura of the other side.

(*A*) *Chemical Pleuritis from Injection of Turpentine.*

EXPERIMENT 23. A dog had been injected on the left side twenty-four hours previously with 3 c.c. of turpentine mixed with 9 c.c. of sterile oil. Animal appeared languid. Ether anesthesia. A mercury manometer was connected with the carotid artery and the respiratory tambour with the breathing cannula, which was inserted in the trachea. After the ether was evenly regulated, a trocar was forced into the right chest in the fifth interspace in the midaxillary line, and the sharp point retracted. The visceral pleura was then scratched with the blunt end of the trocar, with no change in blood pressure. The sharp point also caused no change in pressure when scraped along the visceral or parietal pleura. Three drops of formalin blown through the trocar caused no change in blood pressure, although respirations were slightly slowed. No effect was observed from the trocar irritation of the left visceral and parietal pleura, but the introduction of 2 drops of formalin caused a sudden slowing of the heart with long strokes of the pen (cardio-inhibitory or "vagal" type), with simultaneous slowing of respiration. The effect lasted for a little over a minute (Fig. 2). The chest was then opened by bone-cutting forceps in the median line, and the thoracic viscera exposed. Respirations were maintained by an air pump. This latter procedure lowered the blood pressure from 100 mm. to 70 mm., at which level the tracing remained steady. Mechanical irritation of left and right parietal and visceral pleuræ with blunt and sharp point had no effect on blood pressure. Scratching the pericardium "in situ" set up long drops of "vagal" type, but when the sac was held away from the heart, the irritation had no effect. Laceration of the lung tissue by squeezing in forceps was negative. Electrical irritation (faradic) of left and right visceral and parietal pleuræ was negative. Stimulation of pericardium "in situ" gave "vagal" type of curves identical with those following direct stimulation of the heart muscle, but stimulation of the free pericardium was negative. Chemical irritation of both visceral and parietal pleuræ had no influence on the pressure curve. Thermal irritation by hot iron and ice of left and right parietal and visceral pleuræ did not alter blood pressure. Briefly stated, the only reflex obtained was through irritation of the left pleura by formalin, and this reflex was lost after opening the chest. Postmortem a fairly marked exudate in left side, with fibrinous pericarditis, was found. Right pleura was normal.

EXPERIMENT 24. A dog had been injected twenty-four hours previously in left side with turpentine 2 c.c. and oil 10 c.c. Trocar irritation of both left and right visceral pleuræ, negative. Formalin 2 drops on right visceral pleura caused slowing of respiration and slight fall in blood pressure. The same amount of formalin on left visceral pleura caused slowing and temporary stopping of respiration, with decided fall in blood pressure (20 mm.). Recovery in about one minute. Postmortem: Thin layer of lymph and small amount of purulent exudate on left side, right pleura congested, no exudate.

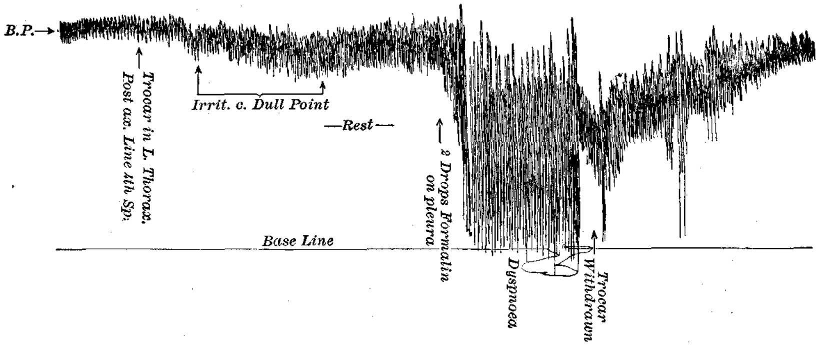

FIG. 2.—*Cardio-inhibitory Reflex.* The upper tracing represents the blood pressure; the base line is below. The inflamed pleura was irritated first with the trocar, then with two drops of formalin. Note the sudden appearance of long and slower strokes after the formalin. Recovery was spontaneous.

EXPERIMENT 25. Left side of chest of dog injected eight hours previously with turpentine 4 c.c. and oil 8 c.c. Blood pressure, 160 mm. Hg. Right visceral pleura repeatedly irritated with sharp point of trocar caused slight slowing of respiration, frequent vagal curves, with a slowing of heart and steady fall in blood pressure to 120 mm. Hg. in the course of two minutes. Rapid recovery to 130 mm. when irritation ceased. Trocar irritation of left visceral pleura slowed respiration slightly, but made no appreciable change in blood pressure. Trocar irritation of right visceral pleura was repeated with fall in blood pressure from 165 to 140 mm. Then both vagi were cut in the neck. The blood pressure fell to 120 mm., then remained steady while respirations were slower. Further irritations of right pleura caused steady fall in blood pressure to 110 mm. with "vagal" strokes. Formalin 4 drops on right visceral pleura negative. Formalin 4 drops on left visceral pleura caused immediately respiratory paralysis and a rapid fall in blood pressure, with death. The cardio-inhibitory curves were set up especially by irritation near root of lungs. Section of vagus nerves failed to destroy entirely the cardio-inhibitory curves or the vasomotor fall. Postmortem: Left pleurisy with thin layer of fibrin and small amount of fluid. Right pleura congested. The abdominal viscera were engorged with blood.

EXPERIMENT 26. Dog was injected six hours before in right chest with turpentine 2 c.c. and oil 6 c.c. Blood pressure, 90 mm. Trocar irritation of left visceral pleura negative. Trocar irritation of right visceral pleura was followed by slight lowering of blood pressure from 90 mm. to 80 mm. and respirations unchanged. Postmortem: Fine fibrinous threads over right pleura. Left pleura normal.

EXPERIMENT 27. Six hours before experiment a small dog was injected in right chest with turpentine 4 c.c. and oil 4 c.c. Blood pressure 100 mm. Trocar irritation of right visceral pleura was negative. Trocar irritation around root of right lung caused the cardio-inhibitory curves. Trocar irritation of left visceral pleura was negative. Formalin 5 drops on left visceral pleura was negative. Formalin 5 drops on right visceral pleura followed by slower and more shallow respirations and by a fall in blood pressure to 76 mm., with long curves. Recovery in about two minutes. Postmortem: Thin pleuritic exudate on right side. Left pleura normal.

EXPERIMENT 28. Dog injected twenty-four hours before in right pleural cavity with turpentine 1 c.c. and oil 6 c.c. Blood pressure, 118 mm. Hg. Trocar irritation of right visceral pleura caused a slight fall in blood pressure. Trocar irritation of left visceral pleura was negative. Formalin 5 drops on right visceral pleura was followed by a gradual rise in pressure from 120 mm. to 134 mm. Formalin 5 drops on left visceral pleura was negative. Postmortem: Right pleuritis with thick fibrinous exudate and free fluid. Left pleura normal.

(*B*) *Bacterial Pleuritis of Twenty-four Hours or Less After Injection of Contaminated Oil.*

EXPERIMENT 29. Twenty-four hours previously dog received injection in the left chest of 5 c.c. of contaminated oil. Blood pressure, 122 mm. Trocar irritation with sharp and dull point of right visceral pleura was negative. Trocar irritation with dull point of left visceral pleura was negative. Trocar irritation with sharp point of left visceral pleura caused a rapid fall in blood pressure from 110 mm. to 64 mm., with shallow respirations. Recovery in two minutes to 80 mm. An injection of 0.5 c.c. of adrenalin in the femoral vein was followed at once by a rise in blood pressure to 200 mm. and the animal recovered (Fig. 3.) Formalin drops 5 on

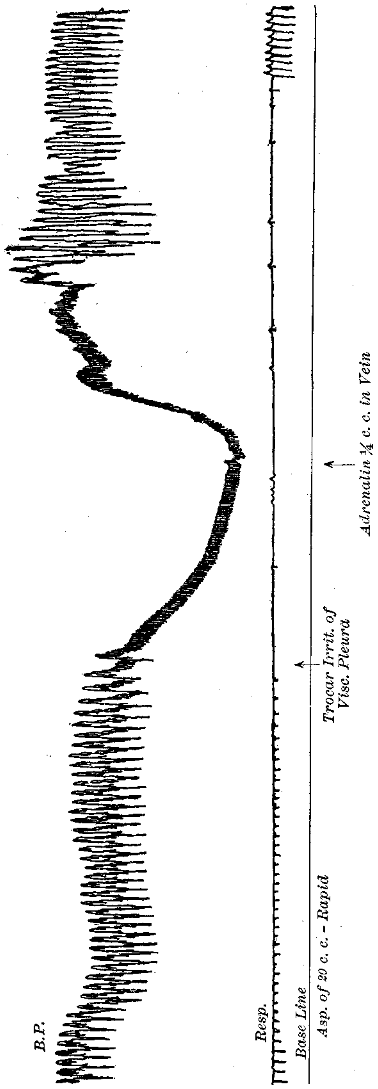

FIG. 3.—*Vasomotor reflex* resulting from scratching the inflamed visceral pleura with a sharp point of the trocar. Respirations ceased simultaneously with the fall in blood pressure. Adrenalin intravenously caused rapid recovery of pressure with gradual return of respirations. Note also the moderate fall in pressure from the rapid withdrawal of fluid.

right visceral pleura was negative. Formalin drops 5 on left pleura caused a slight fall in pressure. Postmortem: Right pleura normal. Left visceral pleura showed a fringe of dense fibrin at edge of lobes, smaller flakes over surface and 100 c.c. of fluid. Evidence of trauma from trocar on middle and upper lobes about an inch from right bronchus. No puncture of lung could be detected.

EXPERIMENT 30. Twenty-four hours previously 5 c.c. of contaminated oil had been injected into the left pleural cavity of a small dog. Trocar irritation with dull and sharp point of right visceral pleura, negative. Trocar irritation with dull and sharp point of left visceral pleura, negative. Formalin 3 drops on right visceral pleura, negative. Formalin 3 drops on left visceral pleura caused a slight fall in blood pressure. With the chest laid open and artificial respiration the same tests were repeated with negative results. Formalin injected directly in the lung tissue on both sides, and compression of lung tissue in the forceps, also were without effect on blood pressure. Post-mortem: Left pleurisy with moderate amount of exudate. Right pleura normal.

EXPERIMENT 31. Into the right chest of a dog 10 c.c. of contaminated oil had been introduced twenty-four hours before experiment. With closed chest the visceral pleura was irritated on both sides with trocar and formalin. Except for a slight fall in blood pressure after applying formalin to the left pleura, the result was nil. Postmortem: Fairly advanced pleurisy on right side. Left pleura normal.

EXPERIMENT 32. To a young dog 8 c.c. of dirty oil was injected in the right thorax twenty-four hours previous to experiment. Scratching the pleural surfaces caused no depression of blood pressure. Application of 5 drops of formalin to the right pleura was followed by a slight fall in blood pressure and slowing of respiration. Both vagi were then cut in the neck. After a period during which the pressure became steady again, 0.5 c.c. of formalin was again applied to the right pleura. Immediately respirations were slowed and the blood pressure fell with long curves from 110 mm. to 40 mm. Recovery was spontaneous. The reflex was not pure vagal, but showed a vasomotor fall as well. Postmortem: Right pleura very congested, but no distinct membrane. Free oil and some purulent exudate in cavity. Left pleura normal.

EXPERIMENT 33. Dog similarly injected in right pleural cavity twenty-four hours before with 200 c.c. of contaminated oil. Rapid aspiration of 150 c.c. of fluid caused a fall in blood pressure from 90 to 70 mm., with gradual recovery to 80 mm. Irritation of right visceral pleura with the trocar produced little change in pressure. Postmortem: Right pleura dotted with fibrin flakes and over 100 c.c. of free fluid present. Left pleura was congested.

(*C*) *Bacterial Pleuritis Forty-eight Hours or More After Injection of Contaminated Oil.*

EXPERIMENT 34. Dog prepared forty-eight hours before by introduction into left chest of 400 c.c. of dirty olive oil. Blood pressure at beginning of experiment was 150 mm. A trocar was inserted in the fifth space, mid-axillary line of the right pleural cavity. Only 2 or 3 c.c. of fluid had escaped when the blood pressure fell rapidly to 56 mm. and the respirations became shallow. Upon withdrawing the trocar the blood pressure quickly went up to 106 mm. when the trocar was reinserted. Again the pressure fell, soon reaching the abscissa line and terminating in death. The trocar could be felt against the visceral pleural membrane, but the amount of friction was not great. Respirations were shallow and slowed, but continued after the pressure reached zero. Postmortem: Left pleural cavity contained about 300 c.c. of oil and purulent exudate. Pleural surface covered with a thick lymph layer. The right cavity held about 50 c.c. of fluid and a thin layer of fibrinous exudate on the lung, which showed two points where the trocar had scratched the pleura. There was slight ecchymosis, but no rupture of the pleura and no evidence of bleeding in the branchioles or pleural cavity. The abdominal viscera were congested to a high degree.

EXPERIMENT 35. Forty-eight hours previously 450 c.c. of dirty oil had been injected into the left thorax of medium-sized dog. Thoracentesis in right fifth interspace, anterior axillary line. When the sharp point of the trocar was moved over the visceral pleura a steady fall in blood pressure took place and continued until death, which occurred in four minutes. Respirations were shallow and slowed, but continued until blood pressure was nearly zero. Postmortem: Left pleura overlaid with a thick fibrinous layer and in the cavity was about 300 c.c. of oil and pus. The right side contained about 100 c.c. of oil and the pleura was thinly concealed by a lymph layer. Near the root of the lung the pleura was discolored as well as posteriorly by the trocar scratch, but no perforation was present. The bloodvessels of the stomach, intestines, and liver were abnormally congested. Brain normal.

EXPERIMENT. 36. For three days 300 c.c. of dirty oil had been present in the left pleural cavity. Irritation of the outer surface of the left visceral pleura with the trocar was negative, but when the trocar scratched the pleura near the root of the lung long "vagal" strokes were produced. Cutting both vagus nerves in the neck seemed to modify these curves, but did not prevent them altogether. Postmortem: Over 300 c.c. of purulent oil in left cavity, with thick plastic layer on pleura. Right pleura also covered with a thick, soft exudate and about 40 c.c. of free fluid in the cavity. No perforation of lung and no hemorrhage was found.

EXPERIMENT 37. Dog had received an injection two days before in left chest of 200 c.c. of dirty oil. A trocar in right pleural cavity in fifth space, anterior axillary line, when moved laterally caused long vertical strokes on the drum, without much influence on the average pressure. On the left side scratching with the trocar was without effect. Postmortem: In the left side of chest was over 200 c.c. of free fluid and a dense pleural membrane. The right lung was covered with a thinner layer of exudate. The heart was displaced to the left. Possibly the trocar touched the pericardium in its movements and thereby set up "vagal" curves.

EXPERIMENT 38. The right thorax of a dog had been injected two days before with 300 c.c. of dirty oil. Trocar irritation of right visceral pleura after withdrawal of 200 c.c. of oil caused practically no change in blood pressure. Trocar irritation of left pleura was followed by a slight fall in pressure. Formalin 2 drops on the left pleura caused great cardio-inhibitory curves, with fall in blood pressure which continued for nearly a minute. Respiration was slowed and labored. Recovery. Postmortem: Right pleura and the pericardium were covered with a thick fibrinous membrane. The left pleura was inflamed and overlaid with a thin, translucent membrane of lymph. The lung tissue puckered where formalin had come into contact with its surface.

EXPERIMENT 39. Dog was injected in the right pleural cavity with 50 c.c. of dirty oil. Mechanical and chemical irritation of pleura were negative. With the chest opened and under artificial respiration, all forms of irritation, mechanical, chemical, thermal, and electrical, were applied to various parts of the pleura with no influence on blood pressure, except over the roots of the lungs, where mechanical and electrical stimulation produced occasional cardio-inhibitory strokes without altering the general level of blood pressure. Postmortem: Right thorax contained about 150 c.c. of turbid oil and over the pleura was a thin, soft exudate. Left lung retracted from pressure of 100 c.c. of fluid and covered with flakes of fibrin. Pericardium concealed by a thick exudate.

EXPERIMENT 40. Dog prepared two days before by introduction of 30 c.c. of contaminated oil into the right pleural cavity. Animal was lively. Stimulation of both pleuræ with the trocar caused only the long strokes that occur physiologically from sweeping along the roots of the lung. Formalin had no effect. Postmortem: Very little inflammation was found in the right side of the thorax and only 50 c.c. of oily fluid. The left pleura appeared normal.

EXPERIMENT 41. Dog forty-eight hours before was injected with 10 c.c. of dirty oil in left chest. Trocar irritation of right visceral pleura with dull point caused only a slight lowering of blood pressure from 126 mm. to 120 mm., but upon scratching the surface with the sharp point the pressure fell rapidly until death took place two minutes later. The respirations simultaneously were slowed and when the pressure reached 50 mm. ceased entirely. Cutting of both vagus nerves in the neck had no apparent effect on the blood pressure (Fig. 4). Postmortem: Pleurisy of high degree on left side, with a thick exudate over the lung. Right pleura much congested, with a few shreds of fibrin on the surface. Slight pericarditis. Evidence of trocar scratches on the right pleura about one inch external to the root of the lung. No perforation of the lung was found.

Experiment 42. In a dog 10 c.c. of dirty oil had been introduced into the left pleural cavity forty-eight hours previously. Irritation of pleuræ on both sides with sharp and dull point produced no change in blood pressure. Formalin injections on the pleuræ were likewise negative. Formalin 1 c.c. sprayed in trachea and bronchial tubes caused a gradual deep fall in pressure from 120 to 6 mm., with slower and deeper respirations. Spontaneous recovery. Postmortem: Left pleura covered with thick layer of lymph and in the cavity 100 c.c. of fluid. Right pleura red and streaked with a few fibrin shreds.

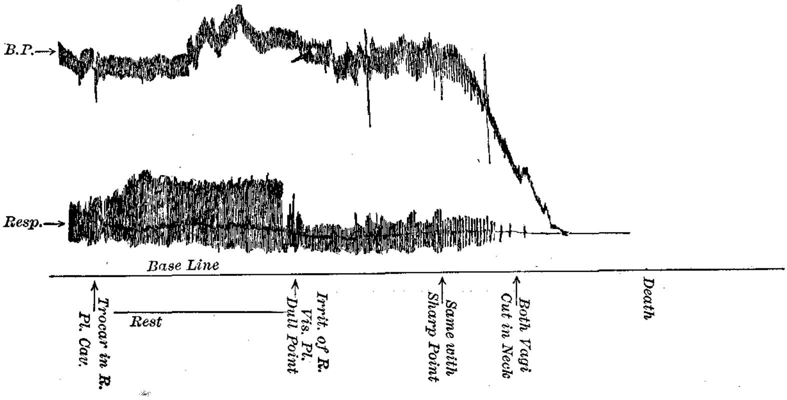

Fig. 4.—*Vasomotor reflex* following irritation of the visceral pleura with a sharp trocar. At the bottom is the base line, the respirations, and at the top the blood pressure tracing. Note rapid fall of pressure and slowing of respirations until death. Section of both vagi in the neck had no effect on blood pressure. Engorgement of abdominal viscera postmortem.

Experiment 43. The dog was injected forty-eight hours before with 8 c.c. of dirty oil in the right pleural cavity. Trocar irritation with dull point of right visceral pleura caused a slight fall in pressure, of the left pleura no change except occasional vagal strokes. Formalin 5 drops on left pleura caused a slight fall in pressure with shallow respirations. The sharp point of the trocar moving over the surface of the left visceral pleura caused slowing of respiration, long "vagal" dips, and a steady fall in pressure from 135 mm. to 80 mm. Then both vagi were cut in the neck without marked effect. By discontinuing the irritation of the pleura the pressure gradually recovered to 110 mm. Further irritation caused shallow breathing and a rapid fall in blood pressure that terminated in death in a minute and a half. Section of the vagi did not prevent the vasomotor reflex. Postmortem: Right pleura covered with thick exudate. Left pleura inflamed and overlaid by a thin film of fibrin. Evidences of trocar scratches and very slight ecchymosis, no perforation. Congestion of abdominal vessels was marked. Brain normal.

Experiment 44. Dog used forty-eight hours after 10 c.c. of dirty oil was introduced into the right pleural cavity. Trocar irritation of right visceral pleura (dull point) caused a moderate fall in blood pressure, with slowing of breathing. By drawing the blunt point over the region of the sympathetic chain, respiration was slowed, then paralyzed, and the pressure curve showed long vagal sweeps with a rapid fall in tension from 100 mm. to 40 mm. Cutting the left vagus had no effect. When the right vagus was also cut the vagal sweeps disappeared and the pressure fell rapidly until death ensued a minute later; that is, the cardio-inhibitory reflex was abolished by section of both vagi, but the vasomotor fall in pressure continued. (Fig. 5). The cardio-inhibitory reflex was therefore central and the impulse to the centre was carried by the vagus nerves. Postmortem: Trocar left "in situ" was found to be pressing directly on the thoracic sympathetic nerve in the sixth space. Also marks of trocar on pleura of middle lobe. Vessels of stomach, intestines, liver, etc., much congested.

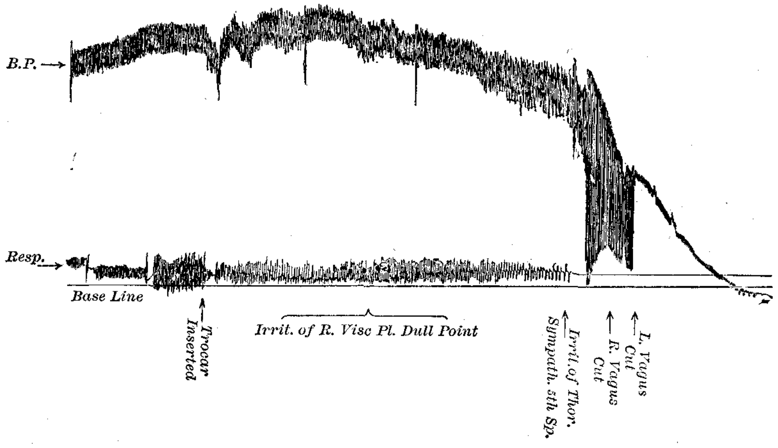

Fig. 5.—*Combined cardio-inhibitory* and *vasomotor reflex* from irritation with a trocar of right thoracic sympathetic nerve in a dog with pleurisy. Upper tracing is blood pressure, lower is respirations, and at bottom the base line. Note gradual fall in pressure from irritating visceral pleura with a dull trocar, then rapid fall with long strokes and cessation of respiration when the nerve trunk is irritated. Section of both vagi in the neck eliminated the cardio-inhibitory strokes, but had no influence on the steady vasomotor fall. Death. Note also the transitory fall in pressure and suspension of respiration when the trocar was forced through the chest wall.

EXPERIMENT 45. The dog forty-eight hours previously had been given 10 c.c. of dirty oil in the right chest. Aspiration of the exudate was accompanied by a fall in pressure from 120 to 110 mm. Trocar irritation of the right and left visceral pleuræ was negative. Formalin 1 c.c. on the right pleura was followed by a slight fall; 1 c.c. of formalin in the left membrane caused a slight rise, then rapid fall from 130 mm. to 14 mm. The type of curve was vasomotor. During the descent of the blood pressure both vagi were cut in the neck, but no effect was seen; 0.5 c.c. of a 1 to 1000 solution of adrenalin injected into the femoral vein caused an instant rise from 16 mm. to 210 mm. Final recovery. During the low tension the respirations were slow and shallow. Postmortem: Right pleurisy marked with thick membrane over lung. Left side contains a small amount of fluid and a beginning pleurisy.

EXPERIMENT 46. Dog prepared by injecting, forty-eight hours previously, 225 c.c. dirty oil in the left pleural cavity. 150 c.c. of fluid aspirated from left side. Trocar irritations of left visceral pleura were negative. Trocar irritation of right visceral pleura showed a gradual fall from 120 mm. to 110 mm. Formalin 1 c.c. in right pleura caused a fall in blood pressure from 116 mm. to 80 mm., with shallow respirations. Recovery. Postmortem: Double pleurisy, more marked on left side.

EXPERIMENT 47. Injection of 200 c.c. of oil in right pleural cavity of dog forty-eight hours previously. 150 c.c. of purulent fluid was removed by aspiration. Atropine 1 mg. was given intravenously, until electrical stimulation of vagus caused no change in the heart action. Formalin 1 c.c. in right visceral pleura caused a vasomotor type of fall in pressure, with slower and shallower respirations. Cutting vagi had no effect on the curve. Death. Postmortem: Right pleurisy, with thick, fibrinous covering. Left pleurisy starting. Engorgement of abdominal viscera.

EXPERIMENT 48. Double pleurisy created in right side of dog by injecting forty hours previously 200 c.c. oil. 100 c.c. exudate aspirated from right side. Formalin 5 drops on right visceral pleura within a minute set up long strokes, with slowing of respiration. At first the blood pressure rose, then fell. Atropine 1 mg. in femoral vein caused an immediate cessation of the "vagal" strokes. Electrical stimulation of vagus in neck gave no reaction. Then 1 c.c. formalin was blown upon left visceral pleura. Soon a vasomotor type of fall in pressure developed and death ensued. Here the atropine abolished the "vagal" reflex, but not the vasomotor. Postmortem: Brain normal. Right pleura covered with thick layer of lymph. Left pleura moderately inflamed. Congestion of abdominal vessels.

EXPERIMENT 49. A double bilateral pleurisy followed forty-eight hours after introducing 200 c.c. of dirty oil in right thorax. After the removal of about 50 c.c. of exudate from the chest the blood pressure showed little change. The application of 0.5 c.c. of formalin to the right visceral pleura caused the long strokes with a mean fall in pressure of about 25 mm. Upon administering a milligram of atropine the long strokes quickly changed to short and more rapid stroke. This experiment indicates that the long strokes were due to excitation of the cardio-inhibitory branches of the vagus, since they disappeared when these fibers were paralyzed by atropine.

EXPERIMENT 50. A dog with a bilateral pleurisy, forty hours after the introduction of 200 c.c. of contaminated oil in the left pleural cavity. Initial blood pressure was 120 mm. After slow aspiration of over 100 c.c. of fluid the pressure was 100 mm. The injection of 1 c.c. of formalin on the left visceral pleura was followed by slow and shallow breathing and by a rapid fall in blood pressure to about 20 mm., with frequent long strokes. Immediate section of both vagus nerves in the neck caused a sudden rise in pressure to 75 mm., with increased rapidity of pulse, but the recovery was only transitory. The second fall was rapid and free from long strokes. Postmortem: About 50 c.c. of fluid in the left cavity and fibrin deposits. Right fibrinous pleurisy, with no free fluid. Engorgement of abdominal bloodvessels. We may infer that two reflexes conspired to depress blood pressure in this experiment; the one acting on the medullary centre through the vagus nerves and eliminated by section of the same; the other, of vasomotor type, causing vasodilatation of the abdominal vessels and not affected by section of the vagi.

EXPERIMENT 51. A dog had been injected in the right pleura over forty hours previous to experiment with 10 c.c. of contaminated oil. About 50 c.c. of exudate was aspirated without any influence on pressure. Then about 200 c.c. of a 1 per cent. formalin solution was forced into the pleural cavity, care being taken to avoid pneumothorax. The fluid was then allowed to flow out by siphonage. The irrigation was accompanied by marked slowing of respiration and a combined type of cardio-inhibitory and vasomotor pulse tracing. Respirations then ceased entirely, section of both vagi in the neck abolished the "vagal" strokes, but the pressure continued to fall until it reached about 10 mm. Hg.; then spontaneously breathing started up again and the blood pressure arose steadily. The animal recovered. (Fig. 6).

SUMMARY OF EXPERIMENTS. Aspiration of oil from the pleural cavity of 6 healthy dogs caused only a slight lowering of blood pressure. Aspiration of oil from the chest of 7 dogs in which pleurisy had been produced caused in 3 little effect, in 3 a considerable fall in pressure and in 1 death.

Irritation of the visceral and parietal pleura in 9 healthy dogs produced no marked effect upon blood pressure.

In the group of 6 pleurisies produced by turpentine 16 per cent. gave a marked blood-pressure-lowering reflex in response to irritation of the trocar, while 50 per cent. gave such a reflex from formalin irritation.

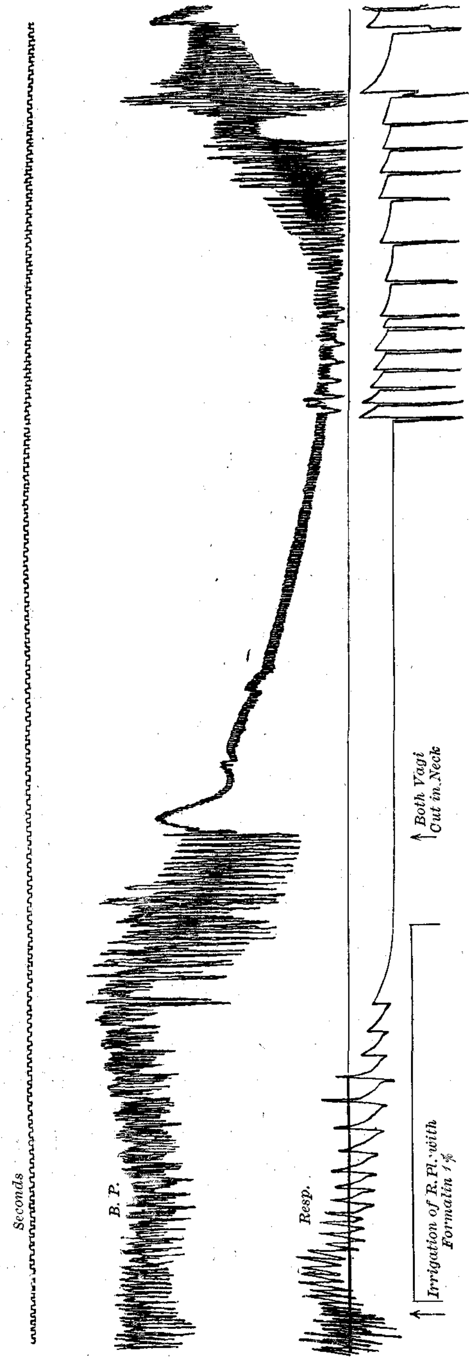

FIG. 6.—*Combined cardio-inhibitory* and *vasomotor reflex* resulting from irrigation with 1 per cent. formalin in glycerin of pleural cavity of dog with artificial empyema. At the top is the time record in seconds. Upper tracing represents blood pressure, the lower respirations, between them the base line. Respirations ceased at beginning of long strokes. Section of both vagi in the neck abolished the long "vagal" strokes, but the vasomotor fall continued. Respirations and blood pressure recovered spontaneously.

Of the group of 5 pleurisies caused by the injection of oil contaminated with bacteria and operated on within twenty-four hours after injection, 20 per cent. showed from the trocar irritation a decided blood-pressure-lowering reflex and 25 per cent. from formalin irritation.

In the group of 17 pleurisies induced by the presence of bacterially contaminated oil in the chest for forty-eight hours or more, 42 per cent. responded to the trocar irritation with a marked depressing reflex and 46 per cent. responded in like manner to the formalin.

Of the total 28 cases of pleurisy of all kinds, 33 per cent. gave a marked blood-pressure-lowering reflex from trocar irritation, while of a total of 17 cases in which formalin irritation was employed, 47 per cent. exhibited a decided fall in blood pressure.

Artificial respiration with the thorax opened tends to abolish all reflexes from irritation of the viscera, as was first pointed out by Brodie and Russell.

It is noteworthy that the trocar irritation seldom gave rise to this reflex in the turpentine pleurisies and in the bacterial pleurisies of short duration, but frequently caused it in the bacterial pleurisies of longer duration. The formalin,[6] on the other hand, induced the reflex in one-half of the turpentine pleurisies and with about the same frequency in bacterial pleurisies of both long and short duration.

Why the reflex occurred in some cases and was entirely lacking in others was explained in part only. In certain instances a very *thick fibrinous exudate* was found, which may have protected the pleura from injury and thus prevented the reflex. But in most cases this variability of reaction was not made clear by anatomical conditions.

The *location* of the irritation was of some importance. The nearer the irritant approached the root of the lung where the fibers of the pulmonary nerves spread out, the more likely was the reflex to occur. The fall in blood pressure arising from mechanical irritation was usually of the vasomotor type; the fall arising from formalin irritation was sometimes of the vasomotor, sometimes of the cardio-inhibitory type, and occasionally seemed to be a combination of both types. It may be noted that the cardio-inhibitory type, though often alarming in its symptoms, never alone caused the death of an animal. The vasomotor type of reflex, however, was always dangerous and several times fatal. Twice death was prevented by adrenalin injections.

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[6] Subsequent experiments indicate that when formalin is introduced in *large quantity*, say 2 to 20 c.c. in the pleural or peritoneal cavity of healthy dogs, a marked lowering of blood pressure often occurs, due in part to absorption in the circulation. We believe, however, that absorption plays a minor rôle when formalin is applied to the visceral pleura in small quantities.

Anatomical Course of the Reflexes. Before discussing the possible courses of these reflexes it seems advisable to review the innervation of the pleura and heart of the dog, and the anatomical arrangement and course of the fibers in the pneumogastric and sympathetic nerves.

The bronchial branches arising from the pneumogastric nerves are given off from the ventral and dorsal aspects of the nerve a little aboral to the aortic arch. The ventral branches pass along the large vessels and accompany the bronchi into the lungs, while the dorsal branches pass along the œsophagus, trachea, and lymph nodes to the root of the lung.

All these fibers unite to form at the root of the lung an extensive network, which is called the pulmonary plexus. The part of the plexus which usually lies upon the principal bronchus and more on the ventral surface is called the anterior pulmonary plexus, while the part lying aboral to the principal bronchus is called the posterior pulmonary plexus. These two plexuses are connected by branches, and the pulmonary is connected with the cardiac plexus.

The stellate ganglion marks the beginning of the thoracic part of the sympathetic ganglionated cord. It is oval and flattened, and lies lateral to the vertebræ upon the m. longus colli at the level of the second rib, and also extends downward to the second intercostal space. From this ganglion are distributed a number of branches, to the first and second thoracic nerves, the lower cervical nerves, and the two cardiac branches (rami accelerantes cordis), which assist in the formation of the cardiac plexus lying upon the lateral surface of the aortic arch and the base of the heart.

The cardiac plexus sends fibers into the pulmonary plexuses above described, from which branches are distributed along the vessels and bronchi to the pleura. Small sympathetic ganglia are interposed at frequent intervals along the nerves. Branches are given off from this plexus, of which the vagus also forms a part, that supply the pericardium and heart muscles. The pleura is innervated therefore by elements of both sympathetic and vagus nerves.

The vasoconstrictor nerves of the body leave the spinal cord by the anterior roots of the spinal nerves from the first dorsal to the third or fourth lumbar inclusive. From the roots they pass by the white rami communicantes to the ganglia of the sympathetic chain lying along the front of the vertebral column. Here they take different courses according to their destinations. The fibers for the head and neck leave by the first four thoracic nerves, pass into the sympathetic chain through the stellate ganglion and the ansa Vieussenii to the inferior cervical ganglion, and up the cervical sympathetic trunk to the superior cervical ganglion. Here they end, and the impulses are carried by a fresh relay of fibers, starting from cells in this ganglion and travel along non-medullated fibers on the walls of the carotid artery and its branches.

The most important vasomotor nerve is the splanchnic nerve. This nerve receives most of the fibers forming the white rami from the lower seven dorsal and upper two or three lumbar roots, the latter fibers often taking a separate course in the lesser splanchnics. The fibers can be seen to pass through the sympathetic chain of the thorax without interruption and for the most part have their cell station in the large ganglia, especially the semilunar ganglia of the solar plexus, whence a thick meshwork of non-medullated fibers is distributed along all the vessels of the abdominal viscera. The area of vessels innervated by this nerve is so large that section of this nerve on each side causes a large fall in general blood pressure.

THE CARDIO-INHIBITORY REFLEX.—The typical cardio-inhibitory reflex obtained by irritation of the inflamed pleura corresponds to that elicited by electrical stimulation of the vagus nerve in the neck. The blood-pressure tracing shows long downward strokes, with a marked difference between systolic and diastolic blood pressures, slowing or temporary arrest of the pulse, and frequently slowing of the respiration. Unless the current is very strong the heart overcomes the inhibitory action and the blood pressure returns to its original level. This reflex was never obtained in healthy dogs by trocar irritation of the pleura or of the thoracic sympathetic nerves. Long, single strokes without slowing of the heart were frequently obtained by scratching the root of the lung or the thoracic portion of the vagus nerve itself or by striking the pericardium with the trocar. These latter curves have very little effect on the mean blood pressure, and because of their slight importance were not recorded as pathological cardio-inhibitory reflexes.

We believe that the cardio-inhibitory reflex resulting from irritation of the inflamed pleura was usually of central origin, arising in the afferent branches of the vagus and travelling upward through the pulmonary ganglia to the combined nucleus of the vagus and accessory nerves in the medulla, the inhibition being transmitted along the accessory fibers to the vagus nerve back to the cardiac plexus and finally to the heart. (Fig. 7.) We believe the reflex to be of central origin, as it was usually absent after section of both vagi.

Atropine in the dosage of 1 mm. injected into a vein either diminished or prevented the reflex.

VASOMOTOR REFLEX. The vasomotor (dilator) reflex differs from the cardio-inhibitory in that the long "vagal" strokes are usually wanting and the mean fall in blood pressure is progressively downward, often resulting in death. The respiration may or may not be slowed. The nature of this reflex may be made clear by the following evidence:

1. Acute engorgement of the vessels of the abdominal viscera was found in all cases, evidently from acute vasodilatation.
2. Section of the vagi in the neck did not prevent the reflex or

alter it after it was induced, which indicates that the reflex was independent of any inhibitory action of the heart.

3. Intravenous injection of adrenalin, a vasoconstrictor, opposed the reflex, causing an immediate rise in blood pressure. Twice the injection of adrenalin solution saved the life of the animal. Atropine, on the other hand, which paralyzes the cardio-inhibitory fibers of the vagus, had no effect.

According to our present knowledge of the course and distribution of the nerves of the sympathetic system it seems probable that this reflex is central rather than peripheral, that is, that the afferent impulse is carried back to the principal vasomotor centre in the medulla or subsidiary centres in the cord, and that the efferent impulses are then transmitted along the white rami to the collateral ganglia. As the reflex is accompanied by such a marked fall in blood pressure it seems probable that the reflex occurs through the principal rather than the subsidiary centres.

The afferent fibers represented in blue (Fig. 8) probably traverse the sympathetic cord, passing upward, downward, and outward without arborizing about these cells in the ganglion and, therefore, without losing their medullary sheath. It is quite generally accepted now that the afferent fibers which are sensory have this arrangement. A reflex beginning in the pleura will traverse these fibers, passing through the posterior root, and the reflex may be established at the level at which the fibers enter the cord, or they may pass upward to arborize about the cells in the principal vasomotor centre in the medulla. This anatomical arrangement precludes the possibility of a more direct reflex arising from the pulmonary plexus and travelling directly along the thoracic ganglionated cord to the splanchnic vessels.

It should be mentioned, however, that Dogiel[7] has described a different arrangement of the fibers in the sympathetic cord, and if his interpretation is correct a peripheral reflex arising in the peripheral plexuses and traversing directly the ganglionated cord is possible.

We have already noted that the effects of this reflex are so general and rapid that it seems probable that the principal vasomotor centre is affected and not the subsidiary centres situated in the cord.

Clinical Observations in Man. The following observations were made in man to ascertain if irritation of the inflamed pleura during thoracentesis produced any marked changes in blood pressure:

Case I.—The patient had a pleurisy with effusion of over two weeks' duration. Thoracentesis in midaxillary line, sixth space. Fluid was seropurulent and contained pneumococci. The initial blood pressure was 100 mm. Hg. After withdrawal of 125 c.c. of fluid the flow ceased. Blood pressure, 98 mm. The trocar was then moved about in the endeavor to start the flow. The visceral pleura was distinctly felt against the trocar during these movements. The blood pressure rapidly fell to 80 mm. when the instrument was withdrawn. In four minutes the blood pressure had risen again to 96 mm.

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[7] Poirier et Charpey, Traité d'anatomie humaine.

CASE II.—Man with a right-sided streptococcic empyema of over a month's duration. Needle inserted near angle of scapula. Initial blood pressure 105 mm. Hg.; after entrance of needle, 98 mm. As no fluid escaped, the needle was moved about and the pleura intentionally scratched with the end. The blood pressure fell immediately to 88 mm. and after a short rest recovered to 94 mm. A few more scratching movements caused a rapid fall to 84 mm. with intermissions of the pulse. Exploratory puncture was then made in the midaxillary line, in the sixth space. Blood pressure after entrance of needle, 90 mm. No fluid was obtained. A few lateral movements of the needle were made against the visceral pleura, when the systolic blood pressure fell to 75 mm., the diastolic pressure below 35 mm., and for a few seconds the pulse could not be felt. Patient felt slight dizziness and faintness. Upon withdrawal of needle the pulse rapidly improved and the subjective symptoms disappeared.

CASE III.—Right pleurisy with bloody effusion. At postmortem a month later, the lung was found retracted and tied down with tuberculous adhesions. Trocar in sixth space, midaxillary line. Initial blood pressure 89 mm. Hg. After insertion of trocar 79 mm. 1200 c.c. of fluid was withdrawn by siphonage without discomfort. Blood pressure, 69 mm. Then the trocar came in contact with the visceral pleura and, although very little more fluid escaped, the blood pressure fell in a few minutes to 57 mm. and the patient complained of faintness, dizziness, and a dull pain at the site of the needle. The pulse beats were very difficult to feel and at times were intermittent. The trocar was removed and in three minutes the blood pressure was 62 mm. Lying down increased blood pressure to 67 mm. Thirty minutes later blood pressure was 80 mm. and the patient was comfortable.

CASE IV.—Left pleurisy of ten days' duration. Thoracentesis in postaxillary line, seventh space. During the withdrawal of 1500 c.c. of fluid by slow siphonage no pain was experienced, and the blood pressure fell from 106 mm. to 100 mm. Scratching the visceral pleura gently with a needle was followed by only slight pain and a fall in blood pressure to 90 mm. In four minutes after needle was removed the blood pressure was up again to 100 mm.

CASES. V, VI, and VII were all acute pleurisies with serous effusions. In all cases there was very little reflex fall of blood pressure from irritating the pleura with the trocar.

CASE VIII.[8]—Man of thirty years with left pleurisy and tuberculosis of the left lung. Thoracentesis in sixth space midaxillary line. Initial blood pressure 120 mm. Hg. After insertion of needle 130 mm. 2000 c.c. of serous fluid aspirated in nine minutes, when blood pressure was 105 mm. The needle end then came suddenly in contact with the visceral pleura and patient complained of dull pain in the epigastrium, but none whatever in the chest. The pain grew rapidly worse and the blood pressure rose steadily to 155 mm. —an increase of 50 mm. in the course of five minutes. Upon withdrawal of the needle the epigastric pain gradually subsided and the blood pressure simultaneously was lowered. Twelve minutes after the maximum anginal pain the blood pressure had returned to 108 mm. and the pain was gone. There is every reason to believe that excitation of the visceral pleura in this instance caused a reflex *vasoconstrictor* action on the abdominal arteries.

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[8] This case was published by Capps, loc. cit.

These observations go to show that in man, as in dogs, irritation of the inflamed pleura often gives rise to a blood-pressure-lowering reflex of cardio-inhibitory or vasodilator type. Also that similar excitation under similar conditions may give rise to a reflex of vasoconstrictor type, with heightening of blood pressure. This latter type of reflex is exceptional and has been observed only in this 1 case out of a total of over 30 patients in whom careful blood-pressure readings have been taken during the progress of aspiration. In our experiments on the pleurisies of animals we have never seen such a striking vasoconstrictor reflex, but several times a gradual rise in blood pressure has followed pleural irritation, which may possibly be explained in this manner.

ILLUSTRATIVE CASES IN LITERATURE. It does not lie within the scope of this paper to discuss the numerous cases recorded in literature of collapse or sudden death occurring in the course of operations in the thorax in which no satisfactory cause could be found postmortem. But it may be pertinent to allude briefly to a few writers who have helped to elucidate the phenomenon.

Sears[9] has recently published a full bibliography besides reporting a case in which death followed fifteen hours after exploratory puncture. Russell[10] described 3 cases, 2 of them children, that died after exploratory puncture and gives the most instructive discussion of the subject at our command. As previously stated he considers that in these cases the needle penetrates the lung tissue and excites vagus nerve endings in the alveoli. He believes that the pleura takes no active part in the reflex—a conclusion entirely opposed to our own. Leichtenstern[11] reports three groups of fatal cases that occurred from operative procedures: 4 patients died suddenly during aspiration; 15 patients died a few minutes to a few days after operation; 5 patients died during irrigation of the pleural cavity, some with partial or general convulsions. Rosenbach[12] reported a sudden death from irrigation of the pleural cavity in a patient with empyema, in which the postmortem findings were entirely negative. He attributed the probable cause of death to irritation of the vagus-nerve endings. He alludes also to an interesting historical case of sudden death resulting from the accidental loss of a part of a syringe in the pleural cavity following an operation for empyema. Auberne[13] describes convulsive attacks accompanying irrigations of the pleura which are sometimes followed by syncope and death, at other times by recovery after a short interval without any bad consequences. Weill[14] refers to similar convulsive movements during irrigation of the chest, especially on the affected side. The convulsions are usually explained by an anemia of the brain which accompanies the reflex fall in the blood pressure (Russell, Rosenbach).

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[9] Trans. Assoc. of Amer. Phys., 1906.

[10] Loc. cit.

[11] Deutsch. Arch. f. klin. Med., 1879, xxv.

[12] Loc. cit.

From these illustrations it is evident that the pleural reflex lowering blood pressure may be caused by a number of forms of irritation of the pleura: (*a*) by irritation or injury of the needle, (*b*) by a foreign body in the pleural cavity; or (*c*) by irrigations of the cavity with antiseptic solutions. Obviously if the susceptibility of the inflamed pleura to dangerous reflexes were fully appreciated, greater care would be used by physicians and surgeons to avoid any unnecessary injury or irritation of the membrane during operations and irrigations.

CONCLUSIONS. 1. Aspiration of oil from the pleural cavity of healthy dogs causes little or no change in the arterial pressure.

2. Aspiration of inflammatory exudate from the pleural cavity of dogs with acute pleurisy often causes a more marked fall in blood pressure. This fall in pressure depends more on the degree of trauma or irritation of the inflamed pleura than on the amount of exudate withdrawn or the rate of withdrawal.

3. Irritation of the visceral pleura of healthy dogs by mechanical, thermal, and electrical means and by certain chemicals, produces little or no effect on blood pressure, except over the roots of the lungs, where mechanical and electrical excitations produce long strokes of vagal type.

4. The effect of irritation of the parietal pleura needs further investigation. The common drop of blood pressure and disturbance of respiration occurring when the trocar is forced through the chest wall into the cavity is probably due to injury of the parietal pleura. The reflex is usually transitory and is seen in both normal animals and in those with pleurisy.

5. In dogs with pleurisy induced by turpentine or by oil contaminated with bacteria, excitation of the inflamed visceral pleura by mechanical and chemical irritants gives varying results. In some cases there is no marked change in blood pressure; in others there is a considerable fall in pressure that may even be fatal.

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[13] Revue de méd. et chir., February, 1879.

[14] Ibid., January, 1887.

6. These reflexes conform to two types, which as a rule occur singly, but may be combined: (*a*) The cardio-inhibitory type, in which the heart is slowed and the pulse tracings make violent excursions with a great range between systolic and diastolic pressure. Respirations also are usually slowed and may be inhibited. This type of reflex when it occurs alone is seldom fatal. (*b*) The vasomotor type, in which the pulse tracings show a steady rapid decline of pressure without a great difference in systolic and diastolic pressure and frequently terminate in death. Respirations as a rule are shallow and may be rapid. In fatal cases the bloodvessels of the abdominal viscera are much engorged from acute vasodilatation. The brain shows no evidence of embolism or hemorrhage.

7. The cardio-inhibitory reflex is central, because it is prevented or stopped by cutting both vagus nerves in the neck. Atropine in a dosage of 1 milligram paralyzes the cardio-inhibitory fibers and destroys the reflex.

8. The vasomotor (dilator) reflex may be central or peripheral. If central, the afferent impulses reach the medulla by way of the thoracic sympathetic, the white rami, and the cord, and not by the vagosympathetic cord. This is proved by the failure of section of the vagosympathetic cord to alter or abolish the reflex. If peripheral, the reflex goes from the pulmonary fibers to the pulmonary plexus, thence to the thoracic sympathetic nerves and downward through the splanchnics to the celiac and other plexuses in the abdomen. This reflex is more direct than the central form, but seems to us inconsistent with the views generally accepted as to the course and direction of impulses in the sympathetic nerves. Adrenalin is the physiological antagonist to the vasodilator reflex and is often life saving. Atropine on the other hand, by its tendency to dilate the cutaneous vessels and lower the mean arterial pressure, seems to intensify the reflex. There is some evidence that the previous administration of atropine modifies the blood pressure—elevating action of adrenalin and thereby deprives it of its full beneficial effect.

9. These types of reflexes occur also in man during operative procedures upon the inflamed pleura. The cardio-inhibitory type is manifested by a slow intermittent pulse, with a great difference between systolic and diastolic pressures; the vasomotor type by a steady fall in blood pressure, without a marked difference in systolic and diastolic pressures, and by a pulse that grows steadily weaker until it cannot be felt.

10. For emergency use in case of falling blood pressure and symptoms of collapse adrenalin intravenously is indicated. Atropine is of little service and may even do harm.

11. Preventive measures come readily to mind. The instrument used in thoracentesis should not irritate the visceral pleura any more than is absolutely necessary. Therefore, the trocar is preferable

to the needle. The trocar should not be inserted at a greater depth than is necessary to obtain fluid. Great care should be employed during the drainage of an empyema, especially to avoid a long projection of the drainage tube inside the cavity. Swabbing the pleural surface is attended with danger. Finally we would emphasize the clinical importance of taking blood-pressure readings at the beginning of and during all operations in the pleural cavity, in order to foresee and thereby prevent the development of a dangerous blood-pressure lowering reflex.

We gratefully acknowledge our indebtedness to Dr. S. A. Mathews, the director of the laboratory, for his constant assistance and encouragement.